REMARKS

Claims 28-46 are pending in this application. Independent claim 28 is amended.

Section 1.b of claim 28 is amended to define more specifically the oligonucleotide mixture specified in the claim by replacing the term "consisting essentially of" with the term "consisting of." No new matter is added

Section (2) of claim 28 is amended to specify "detecting stable hybrids formed during the incubation, wherein a hybridization signal indicating the formation of a hybrid or lack of formation of a hybrid after a single round of hybridization at the distinct location is indicative of a genotype of the individual." Support for the amendment is found in the Specification at page 3, lines 3-4 ("[g]enotyping information for the multiple samples is then derived simultaneously by reading the microarray signals"). Further support is found in page 9, lines 17-18, page 14, lines 5-12 and page 15 lines 18-20.

Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

Reconsideration is respectfully requested in view of the following remarks. For the Examiner's convenience and reference, Applicant's remarks are presented in the order in which the corresponding issues were raised in the Office Action. Reconsideration is respectfully requested in light of the above amendments and the following remarks.

I. Examiner's Interview

Applicant thanks the Examiner for the telephonic interview with Applicant's representatives Shantanu Basu and Gene Yee conducted on August 4, 2003. Applicant's representatives thank the Examiner for her many helpful suggestions in identifying claim languages that were causes of concern and her suggestions for rectifying them.

II. Interpretation of the claim language "consisting essentially of"

The Examiner rejected Applicant's argument from the previous Office Action response that the universal probe set taught by Drmanac is excluded from the previously claimed oligonucleotide mixture which recited in part, "the oligonucleotides in the probe mixture consist essentially of ..."

The Examiner based her rejection of this argument on her construction of the term "consisting essentially of" as being equivalent to "comprising." (Office Action of June 5, 2003, page 14).

Applicant respectfully traverses the Examiner's construction of the phrase "consisting essentially of" in the context of the pending claims. Applicant does not agree that the term "consisting essentially of" is construed to be equivalent to "comprising." (A "consisting essentially of" claim occupies a middle ground between closed claims that are written in a "consisting of" format and fully open claims that are drafted in a "comprising" format." PPG Industries v. Guardian Industries Corp., 156 F.3d 1351, 1354 (Fed. Cir. 1998); internal citations omitted).

The Examiner cites to a section of the MPEP which states: ""for the purposes of searching for and applying prior art absent a clear indication in the specification or claims of what the basic and novel characteristics are, "consisting essentially of" will be construed as equivalent to comprising." (emphasis added). This section of the MPEP refers to the PPG Industries case.

The Federal Circuit states that "consisting essentially of" means that "the claimed glass invention has in it the ingredients that are specifically identified in the claim ... [o]ther ingredients may also be present in the glass, although not specifically identified in the claim, so long as those other unlisted ingredients do not have a material effect on the basic and novel characteristics of the glass." PPG Industries at 1354. (emphasis added.). In PPG Industries, the Federal Circuit noted that in that specific fact pattern, there was inherent imprecision resulting from the use of the term "consisting essentially of."

Applicant submits that there is no such ambiguity as to the basic and novel characteristics of the oligonucleotide mixture. The oligonucletide mixture is clearly recited in claim 28 to be "oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which a genotype is to be determined, wherein the oligonucleotides ... [have] ... sequences complementary to a segment containing the marker for (1) a gene, (2) one or more allelic variants of the gene, and (3) a gene and one or more allelic variants of the gene." Because of there is no ambiguity about the basic and novel characteristics of the oligonucleotides, Applicant submits that "a clear indication in the specification or claims of what the basic and novel characteristics" is present and the conditions specified in the

MPEP for construing the term "consisting essentially of" as being equivalent to "comprising" are not met. Applicant respectfully requests that the Examiner interpret the term "consisting essentially of" in accordance with its established definition.

Solely in the interest of furthering prosecution, and without conceding the Examiner's construction of the phrase "consisting essentially of," Applicant has amended Claim 28 to recite, in part, "the oligonucleotides in the probe mixture consist of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which a genotype is to be determined, wherein the oligonucleotides complementary to the polynucleotides are selected from the group consisting of oligonucleotides with sequences complementary to a segment containing the marker for (1) a gene, (2) one or more allelic variants of the gene, and (3) a gene and one or more allelic variants of the gene, and also consisting essentially of, optionally, control oligonucleotides." (emphases added).

Should the Examiner find the Applicant's argument persuasive with respect to the interpretation of the term "consisting essentially of," Applicant requests the Examiner to inform Applicant of her decision and allow Applicant an opportunity to further amend the claims and restore the term "consisting essentially of."

Applicant reserves the right to pursue claims directed to an oligonucleotide mixture consisting essentially of the named ingredients in pending claim 28 in a continuing or divisional application.

III. Claim Rejections Under 35 U.S.C. § 102

Claims 28-34, 36-39, 41-42 and 46 stand rejected under 35 U.S.C. 102(b) as being anticipated by Shuber (U.S. Patent No. 5,834,181, issued 10 November 1998). The Examiner cites Shuber for disclosing a method of simultaneously genotyping multiple samples, wherein the method comprises a single round of hybridization.

The Examiner concedes that the method disclosed by Shuber involves a subsequent sequencing step to identify the hybridizing material. (*See* Office Action at page 4). However, the Examiner asserts that because the Applicant's instant claims are drawn to a method "comprising" the steps of incubating and detecting that such claim language would encompass the additional

sequencing step in Shuber. (*See* Office Action at page 4).

In response, Applicant amends claim 28 to specify a method that allows "detecting stable hybrids formed during the incubation, wherein a hybridization signal indicating the formation of a hybrid or lack of formation of a hybrid after a single round of hybridization at the distinct location is indicative of a genotype of the individual." (emphasis added). By this amended language, Applicant clarifies that detection of the hybridization signal (or lack thereof) is sufficient to identify the genotype of the sample and no additional steps are needed.

In contrast, the method disclosed in Shuber does not disclose a determination of genotype by detecting a hybridization signal. Rather, Shuber teaches hybridization with radiolabeled oligonucleotides and detection of hybridization by autoradiography. Following detection of hybridization, "[t]he specific mutation present in any pool-positive sample [is] identified by eluting the hybridized oligonucleotide from the sample DNA and directly interrogating the oligonucleotide sequence." (Shuber, column 13, lines 2-5). Thus, Shuber discloses genotyping by sequence analysis following the hybridization step.

Since Shuber does not disclose the determination of genotype by detection of "a hybridization signal indicating the formation of a hybrid or lack of formation of a hybrid" as specified in independent claim 28, as amended, Shuber fails to teach each and every element of claim 28.

Claims 31-34, 36-39, 41-42 and 46 depend from independent claim 28 and Shuber does not anticipate claim 28. Therefore, Applicant submits that Shuber does not anticipate amended, independent claim 28 and dependent claims 31-34, 36-39, 41-42 and 46 and respectfully request that the rejection under 35 USC sec.102 be withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 103

(i) Claims 35 and 43-45 stand rejected under 35 U.S.C. § 103 as being unpatentable over Shuber in view of Drmanac.

Drmanac is cited for disclosing array densities of 1000 locations/cm^2.

The Examiner acknowledged previously that the Drmanac reference teaches a "method

comprising multiple rounds of hybridization wherein e.g. a round hybridizes with positive probes and a subsequent round hybridizes with negative probes but Drmanac does not teach detection of the hybrid following a single round of hybridization is indicative of a genotype." (emphasis added, Office Action of March 4, 2003 (Paper No. 24) at 7). Thus, the Examiner agrees that Drmanac, unlike the instant claims, does not teach a single round of hybridization to perform genotyping. Rather, the Drmanac method requires multiple rounds of hybridization to reveal genotype.

As explained above in response to the 35 U.S.C. § 102 rejection, Shuber does not teach each and every element of claim 28. In particular, Shubert fails to teach the determination of genotype by detection of "a hybridization signal indicating the formation of a hybrid or lack of formation of a hybrid" as specified in amended, independent claim 28. Drmanac also does not teach this limitation. Since Shuber and Drmanac, by themselves or in combination, do not teach each and every limitation of claim 28, Applicant respectfully requests withdrawal of these grounds for rejection for claims 35 and 43-45.

(ii) Claim 40 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Shuber in view of Hames. Claim 40 depends from independent claim 28.

Hames is cited for disclosing hybridization at about 10°C below the melting temperature.

As discussed above, Shuber does not teach all limitations of independent claim 28. In particular, Shubert fails to teach the determination of genotype by detection of "a hybridization signal indicating the formation of a hybrid or lack of formation of a hybrid" as specified in independent claim 28, as amended. Hames also does not teach or suggest this limitation. Claim 40 depends from independent claim 28 and Shuber and Hames, by themselves or in combination, do not teach each and every limitation of claim 28. Therefore, Applicant respectfully requests withdrawal of this ground for rejection.

(iii) Claims 28-39 and 41-46 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Drmanac in view of Brown.

The Examiner acknowledges that Drmanac teaches a "method comprising multiple rounds of hybridization" and Drmanac "does not teach detection of the hybrid following a single round of

hybridization is indicative of genotype." (emphasis added, Office Action of June 5, 2003, page 11). However the Examiner states that genotyping *comprising* a single round of hybridization was well-known in the art and cites Brown et al. in support.

The Examiner cites Brown for the teaching of "detecting stable hybrids following a single round of hybridization which is indicative of a genotype." The Examiner argues that it would have been obvious to apply the differentially labeled probes of Brown et al. to the method of Drmanac to permit simultaneous detection of multiple samples following a single hybridization step. (Office Action of June 5, 2003, page 11).

Applicant's previously submitted arguments (submitted May 5, 2003) that the claimed probes are limited to the novel probe mixture by the claim language "oligonucleotides in the probe mixture consist essentially of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which a genotype is to be determined" (emphasis added), wherein the oligonucleotides have "sequences complementary to a segment containing the marker for (1) a gene, (2) one or more allelic variants of the gene, and (3) a gene and one or more allelic variants of the gene." The Examiner rejected the argument based on her interpretation of the claim term "consist essentially of" as being equivalent to "comprising." (Office Action of June 5, 2003, page 14).

In section II above, Applicant has noted their grounds for traverse based on the legal interpretation of the claim term "consisting essentially of." However, solely to expedite prosecution of this Application, Applicant amends claim 28 to read "oligonucleotides in the probe mixture consist of ... wherein the oligonucleotides complementary to the polynucleotides are selected from the group consisting of oligonucleotides with sequences complementary to a segment containing the marker for (1) a gene, (2) one or more allelic variants of the gene, and (3) a gene and one or more allelic variants of the gene." Applicant submits that by this amendment the oligonucleotides are limited to the novel probe mixture specified in claim 28, as amended.

Amended independent claim 28 recites "the oligonucleotides in the probe mixture consist of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which a genotype is to be determined,

wherein the oligonucleotides complementary to the polynucleotides are selected from the group consisting of oligonucleotides with sequences complementary to a segment containing the marker for (1) a gene, (2) one or more allelic variants of the gene, and (3) a gene and one or more allelic variants of the gene, and optionally, control oligonucleotides." Drmanac teaches a universal probe set. Neither Drmanac nor Brown et al. teach the specific probe mixture specified in claim 28, as amended.

Further, Applicant submits that neither Brown et al. nor Drmanac teach or suggest a second limitation of claim 28, namely "detecting stable hybrids formed during the incubation, wherein a hybridization signal indicating the formation of a hybrid or lack of formation of a hybrid after a single round of hybridization at the distinct location is indicative of a genotype of the individual," as further specified in amended claim 28.

Drmanac and Brown et al., individually or in combination, do not teach each and every element of independent claim 28, as amended. Claims 29-39 and 41-46 depend from claim 28. Therefore, Applicant respectfully requests that the rejection of claims 28-39 and 41-46 based on Drmanac and Brown et al. under 35 U.S.C. § 103(a) be withdrawn.

(iv) Claim 40 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Drmanac in view of Brown as applied to Claim 28 and further in view of Hames.

Hames is cited for teaching hybridization at 10°C below melting temperature. Hames does not teach or suggest either the specific oligonucleotide probe mixture or the determination of genotype by detection of hybridization signal. As discussed above in section IV.(iii), neither Drmanac nor Brown et al. teach or suggest the two limitations of claim 28, as amended. Thus Hames, Drmanac and Brown et al., individually or in combination, do not teach or suggest all the elements of independent claim 28. Claim 40 depends from independent claim 28 and includes all limitations specified in claim 40. Thus, Applicant respectfully requests withdrawal of this ground for rejection of claim 40 over Hames, Drmanac and Brown et al under 35 U.S.C. § 103(a).

CONCLUSION

In light of the arguments set forth above, Applicant earnestly believes that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **529492000100**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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